

Listing of the claims

1. (previously presented) A method of modulating expression of an endogenous cellular gene in a cell, the method comprising the step of:

contacting the cell with a first polynucleotide encoding a first zinc finger protein, wherein the first zinc finger protein is a fusion protein comprising a designed or selected zinc finger protein in operative linkage with a functional domain, further wherein the fusion protein binds to a first target site in the gene;

thereby modulating expression of the endogenous cellular gene.

2. (previously presented) The method of claim 1, wherein the step of contacting further comprises contacting the cell with a second polynucleotide encoding a second zinc finger protein that binds a second target site in the endogenous cellular gene.

3. (original) The method of claim 2, wherein the first and second target sites are adjacent.

4. (original) The method of claim 3, wherein the first and second zinc finger proteins are covalently linked.

5. (original) The method of claim 1, wherein the first zinc finger protein is a fusion protein comprising at least two regulatory domains.

6. (original) The method of claim 3, wherein the first and second zinc finger proteins are fusion proteins, each comprising a functional domain.

7. (previously presented) The method of claim 6, wherein the first and second zinc finger proteins are fusion proteins, each comprising at least two functional domains.

8. (previously presented) The method of claim 1, wherein the cell is selected from the group consisting of an animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal cell.
9. (original) The method of claim 8 wherein the cell is a plant cell.
10. (original) The method of claim 8, wherein the cell is a mammalian cell.
11. (original) The method of claim 10, wherein the cell is a human cell.
12. (original) The method of claim 1 wherein the expression of the endogenous cellular gene is repressed.
13. (original) The method of claim 12, wherein the functional domain is selected from the group consisting of unliganded thyroid hormone receptor (TR), v-erbA, Dax, RBP, MeCP2, MBD2B and a DNMT.
14. (original) The method of claim 1, wherein the expression of the endogenous cellular gene is activated.
15. (original) The method of claim 14, wherein the functional domain is ligand-bound thyroid hormone receptor.
16. (original) The method of claim 15, wherein the ligand is 3,5,3'-triiodo-L-thyronine (T3).
17. (original) The method of claim 1 wherein the functional domain is a bifunctional domain (BFD).

- 18.** (original) The method of claim 17, wherein the activity of the bifunctional domain is dependent upon interaction of the BFD with a second molecule.
- 19.** (original) The method of claim 18, wherein the BFD is selected from the group consisting of thyroid hormone receptor, retinoic acid receptor, estrogen receptor and glucocorticoid receptor.
- 20.** (original) The method of claim 18, wherein the second molecule is a protein.
- 21.** (original) The method of claim 18, wherein the second molecule is a small molecule.
- 22.** (original) The method of claim 19, wherein the second molecule is a small molecule.
- 23.** (original) The method of claim 22, wherein the small molecule is selected from the group consisting of thyroid hormone (T3), all-*trans*- retinoic acid, estradiol, tamoxifen, 4-hydroxy-tamoxifen, RU-486 and dexamethasone.
- 24.** (canceled)
- 25.** (previously presented) The method of claim 1, wherein sequences encoding the first zinc finger protein are operably linked to a promoter, and wherein the first polynucleotide is administered to the cell in a lipid:nucleic acid complex or as naked nucleic acid.
- 26.** (previously presented) The method of claim 1, wherein sequences encoding the first zinc finger protein are contained in an expression vector and are operably linked

to a promoter, and wherein the method further comprises the step of first administering the expression vector to the cell.

27. (original) The method of claim 26, wherein the expression vector is a viral expression vector.

28. (original) The method of claim 27, wherein the expression vector is selected from the group consisting of a retroviral expression vector, an adenoviral expression vector, and an AAV expression vector.

29. (previously presented) The method of claim 25, wherein the promoter is an inducible promoter.

30. (previously presented) The method of claim 26, wherein the promoter is an inducible promoter.

31. (previously presented) The method of claim 1, wherein the first target site is upstream of a transcription initiation site of the endogenous cellular gene.

32. (previously presented) The method of claim 1, wherein the first target site is adjacent to a transcription initiation site of the endogenous cellular gene.

33. (previously presented) The method of claim 1, wherein the first target site is downstream of a transcription initiation site of the endogenous cellular gene.

34. (original) The method of claim 1, wherein the zinc finger protein comprises an SP-1 backbone.